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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

GlaxoSmithKline
Corporate IP

29 JUL 2004

PCT

To:

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| Received Stevenage Corporate IP | Received BRENTFORD |
| 28 JUL 2004 | 28 JUL 2004 |
| ATTY: SAL/SDA P.M.: N/A ATTY CHECKED/FILED | AMT Date of mailing (day/month/year) |
| 26.07.2004 | |

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Applicant's or agent's file reference
SALPF4813

IMPORTANT NOTIFICATION

| | | |
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| International application No. PCT/EP 03/06417 | International filing date (day/month/year) 18.06.2003 | Priority date (day/month/year) 19.06.2002 |
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Applicant
SMITHKLINE BEECHAM CORPORATION et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annex, if any, is being transmitted to the International Bureau for communication to all the elected C.
3. Where required by any of the elected C, the International Bureau will prepare an English translation of the report (but not of any annexes) and transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international
preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized Officer

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PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference SAL/PF4813 | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No. PCT/EP 03/06417 | International filing date (day/month/year) 18.06.2003 | Priority date (day/month/year) 19.06.2002 |
| International Patent Classification (IPC) or both national classification and IPC C07D271/06 | | |
| Applicant SMITHKLINE BEECHAM CORPORATION et al | | |

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| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application</p> |

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| Date of submission of the demand 29.12.2003 | Date of completion of this report 26.07.2004 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Gavriliu, D Telephone No. +49 89 2399-8274 |



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/06417

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-85 as originally filed

Claims, Numbers

1-26 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/06417

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
 - the entire international application,
 - claims Nos. (1-8,13-25)all partly and 25,26(IA)
because:
 - the said international application, or the said claims Nos. 25 and 26(IA) relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - no international search report has been established for the said claims Nos. (1-8,13-25)all partly
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
 - the written form has not been furnished or does not comply with the Standard.
 - the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|------|--------|------|
| Novelty (N) | Yes: | Claims | 1-26 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-26 |
| Industrial applicability (IA) | Yes: | Claims | 1-24 |
| | No: | Claims | |

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/06417

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

For reasoning with regards to unsearched subject-matter, see Form PCT/ISA/210 of the International Search Report. No International Preliminary Examination will be carried out with respect to subject-matter which is not covered by the search report (Rule 66.1(e)PCT).

Claims 25,26 relate to subject-matter considered by this Authority to be covered by the provision of Rule 67.1(iv)PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claims(article 34(4)(a)(I)PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

- D1: WO 01/40207 A (SIERRA MICHAEL LAWRENCE ;GLAXO GROUP LTD (GB)) 7 June 2001 (2001-06-07)
- D2: WO 02/46174 A (GELIBERT FRANCOISE JEANNE ;GLAXO GROUP LTD (GB); LIU KEVIN GUANGC) 13 June 2002 (2002-06-13)
- D3: WO 02/14291 A (NIPPON CHEMIPHAR CO., LTD., JAPAN) 21 February 2002 (2002-02-21)
- D4: EP-A-1 067 109 (ONO PHARMACEUTICAL CO) 10 January 2001 (2001-01-10)

2. Novelty (Article 33(1) and (2)PCT)

The subject-matter of the Claims 1 to 25 is novel over the cited documents on the account of the spacer group linking the phenoxy and the heteroaryl moieties of the claimed derivatives- compare the present linking group -CH2N(R5)-(CH2)n- to -(CH2)n-X²-(C=O)-(D1); X²-(CnH2n)-(D2); X²-Y-X¹- (D3); -A2-A1-(D4).

3. Inventive step (Article 33(1) and (3)PCT)

The application is concerned with compounds that activate human peroxisome

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/06417

proliferator activated receptor (hPPARs). D1-D4 disclose hPPAR activators.

In view of the prior art, the technical problem underlying the application is seen in the provision of further hPPAR activators.

D1 is considered to represent the closest prior art. Compound of example 3 disclosed on page 40 of D1, which can be regarded as one of the structurally closest prior art hPPAR activators, differs from the claimed compounds only on account of the replacement in the spacer group of carbonyl with methylene. D2-D4 teach that the spacer group can vary with the retention of the activity. Accordingly, the skilled person faced with the problem of finding further hPPAR activators would have arrived at the claimed compounds, since their activity as hPPAR activators could have been expected in the light of the prior art having regard to the minimal structural difference between the claimed derivatives and those of D1. The subject-matter of Claims 1-26 lacks therefore an inventive step.